ABSTRACT

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Title of Thesis: Iron-chelating properties of selected novel chelators from 4-acyl-5-pyrazolone group II

Iron deficiency and iron overload play important roles in the pathophysiology of certain human diseases. Administration of iron chelators is a suitable therapy in iron overload conditions, especially in cases of hematological diseases treated with blood transfusions. Iron-chelating therapy appears as well as a promising tool for other diseases (acute myocardial infarction, tumor, etc.). Several factors should be considered according to expected indications: 1) oral efficiency, 2) activity in acidic environment, 3) ability to reduce ferric ions to ferrous ions (risk of pro-oxidation).

The aim of this thesis was to verify the iron-chelating properties of selected novel chelators from 4-acyl-5-pyrazolone group by use of UV-VIS spectrophotometric methods. From this group, p-terc.butyl- and p-nitroderivatives of the basic structure and the derivatives marked as H_2Q3Q and H_2QPy, which are double molecules of the basic structure, were chosen.

All of the tested substances had some potential to chelate ferrous ions and were also devoid of the ability to reduce ferric ions. The most effective chelator was H_2Q3Q that had high and the same affinity for ferrous ions in all patophysiologically important pHs (4.5-7.5) and for ferric ions at pH 4.5 with the probable stoichiometric ratio of 3:2. Terc.butyl- and nitroderivatives were unambiguously less effective in the chelation of ferrous ions. But their ability to bind ferric ions at pH 4.5 approached that of H_2Q3Q. In the case of H_2QPy, it was on the contrary shown, that its affinity to ferrous ions decreased with increasing pH. But neither at the lowest tested pH 4.5, H_2QPy was more efficient than H_2Q3Q or terc.butylderivative.

The results show that H_2Q3Q and H_2QPy have the potential to be suitable iron chelators. Very interesting is especially H_2QPy, which has higher affinity for iron at acidic than at neutral pH. On the other side, it is necessary to mention, than H_2QPy is rather a prototype, because its iron-chelating properties are relatively weak.

KEYWORDS:

Iron, iron chelators, 4-acyl-5-pyrazolones